

File 348:European Patents 1978-2000/Mar W02
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File 349:PCT FULLTEXT 1983-2000/UB=, UT=20000210
(c) 2000 WIPO/Micropatent

Set	Items	Description
S1	9959	IFN OR INTERFERON
S2	136477	TYPE() I OR ALPHA OR BETA
S3	43848	RECEPTOR?
S4	22	IFNAR?
S5	471	(S1(4N)S3 AND S2) OR S4
S6	214668	COMPLEX OR CONJUGATE OR FUSION OR FUSED
S7	62	S5 AND S6(2N)S1
S8	295950	COMPLEX? OR CONJUGAT? OR FUSION? OR FUS
S9	442	ALENT? OR CROSS()LINK?
S10	598	S5 AND S8
S11	5487	S1/TI
S12	12153	S3/TI OR S4/TI
S13	2	S8/TI
S14	21	S10 AND S11 AND S12
	22mar00 13:28:38	S10 AND S11 AND S8
	22mar00 11:47:04	

S11	5487	S3/TI OR S4/TI
S12	12153	S8/TI
S13	2	S10 AND S11 AND S12
S14	21	S10 AND S11 AND S8
	22mar00 13:28:38	22mar00 11:47:04

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(c) 2000 Cambridge Sci Abs

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S8 2926 SOLUBLE (2N) S3
S9 68 S5 AND S8
S10 2 S9 AND DT=REVIEW
22mar00 15:20:06

	L #	Hits	Search Text	DBs
1	L1	7743	interferon or ifn	USPAT
2	L2	186	(1 adj3 receptor\$1) or ifnar\$2	USPAT
3	L3	223531 0	3.clm.	USPAT
4	L5	24	(IFNAR\$2 OR (1 ADJ3 RECEPTOR\$1)).clm.	USPAT

USES THEREOF

PROTEINE CHIMERE DU RECEPTEUR D'INTERLEUKINE-6 SOLUBLE/LIGAND, ANALOGUES DE
 CELLE-CI ET APPLICATIONS
 Patent Applicant/Assignee:
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Patent and Priority Information (Country, Number, Date):

Patent: WO 9902552 A2 19990121
 Priority Application: WO 9811321 19980709 (PCT/WO IL9800321)
 Designated States: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU;
 CZ; DE; DK; EE; ES; FI; GB; GE; GH; GM; HR; HU; ID; IL; IS; JP; KE; KG;

KP; KR; KZ; LC; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ;
 PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ;
 YU; ZW; GM; KE; LS; MW; SD; SZ; UG; ZW; AM; AZ; BY; KG; KZ; MD;
 TJ; TM; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC;
 PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; GW; ML; MR; NE; SN; TD; TG

Publication Language: English

Filing Language: English

Fulltext Word Count: 16466

English Abstract

Chimeric proteins constructed from the fusion of the naturally
 occurring form of the soluble IL-6 receptor and IL-6 which are useful for
 treatment of cancer and liver disorders, enhancement of bone marrow
 transplantation, and treatment of other IL-6 related conditions are
 provided.

French Abstract

Ces proteines chimeres obtenues grace a la fusion de la forme d'origine
 naturelle du recepteur d'IL-6 soluble et d'IL-6, se revelent efficaces en
 matiere de therapie anticanceruse et de traitement de troubles
 hepatiques, d'amelioration de la greffe de moelle osseuse ainsi que de
 traitement d'autres troubles lies a l'IL-6.

12/3,AB/118 (Item 12 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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105224075 CA: 122(21)263315b JOURNAL

Logy model of human interferon-.alpha.8 and its receptor complex

AUTHOR(S): Seto, Marian H.; Harkins, Richard N.; Adler, Marc; Whitlow,

Marc; Church, Bret W.; Croze, Ed

LOCATION: Protein Biochem. Biophys., Berlex Biosci., Richmond, CA, 94804,

USA

JOURNAL: Protein Sci. DATE: 1995 VOLUME: 4 NUMBER: 4 PAGES: 655-70

CODEN: PRGIEI ISSN: 0961-8368 LANGUAGE: English

12/3,AB/128 (Item 22 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

(c) 2000 American Chemical Society. All rts. reserv.

105224075 CA: 105(25)224075c JOURNAL

Extraction of alpha interferon-receptor complexes with digitonin

AUTHOR(S): Eid, Pierre; Mogensen, Knud Erik

LOCATION: Lab. Oncol. Virale, Inst. Rech. Sci. Cancer, 94802, Villejuif,

Fr.

JOURNAL: Methods Enzymol. DATE: 1986 VOLUME: 119 NUMBER: Interferons,

Pt. C PAGES: 347-51 CODEN: MENZAU ISSN: 0076-6879 LANGUAGE: English

12/3,AB/129 (Item 23 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

(c) 2000 American Chemical Society. All rts. reserv.

104086869 CA: 104(11)86869r JOURNAL

Receptors for human interferon-alpha: two forms of interferon-receptor
 complexes identified by chemical cross-linking

AUTHOR(S): Raziuddin, Arati; Gupta, Sohan L.

LOCATION: Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA

JOURNAL: Prog. Clin. Biol. Res. DATE: 1985 VOLUME: 202 NUMBER: 2-5A

Syst. PAGES: 219-26 CODEN: PCBRD2 ISSN: 0361-7742 LANGUAGE: English

File 34:SciSearch(R) Cited Ref Sci 1990-2000/Mar W2

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File 73:EMBASE 1974-2000/Mar W1

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File 155:MEDLINE(R) 1966-2000/May W2

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File 5:Biosis Previews(R) 1969-2000/Mar W3

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File 349:PCT FULLTEXT 1983-2000/UB=, UT=20000210

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File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

File 654:US Pat.Full. 1990-2000/Mar 14

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File 76:Life Sciences Collection 1982-2000/Jan

(c) 2000 Cambridge Sci Abs

File 399:CA SEARCH(R) 1967-2000/UD=13212

(c) 2000 American Chemical Society

File 348:European Patents 1978-2000/Mar W02

(c) 2000 European Patent Office

Set	Items	Description
S1	367242	IFN OR INTERFERON
S2	4220248	TYPE(I) I OR ALPHA OR BETA
S3	2822197	RECEPTOR?
S4	591	IFNAR?
S5	11193	(S1(4N)S3 AND S2) OR S4
S6	2964113	COMPLEX OR CONJUGATE OR FUSION OR FUSED
S7	463	S5 AND S6(2N)S1
S8	308	RD (unique items)
S9	62	S8/1996-1997
S10	2172243	S6/TI OR S6/AB
S11	164	S8 AND S10
S12	132	S11 NOT S9

12/3,AB/21 (Item 21 from file: 34)
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
 (c) 2000 Inst for Sci Info. All rts. reserv.

0388508 Genuine Article#: QN635 Number of References: 49
 Title: CHARACTERIZATION OF A DOMAIN OF A HUMAN TYPE- I INTERFERON
 RECEPTOR PROTEIN INVOLVED IN LIGAND-BINDING
 Author(s): EID P; TOVEY MG
 Corporate Source: INST RECH CANC, VIRAL ONCOL LAB, CNRS, UPR 9045, 7 RUE GUY
 MOQUET BP8/F-94801 VILLEJUIF/FRANCE/
 Journal: JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, 1995, V15, N3 (MAR)
 ,P205-211
 ISSN: 1079-9907
 Language: ENGLISH Document Type: ARTICLE
 Abstract: Two monoclonal antibodies that recognize different epitopes of
 the extracellular domain of one of the proteins that constitute the
 type I interferon receptor were used to delineate the interferon
 binding site. Antibody 64G12 both inhibits the binding of radiolabeled
 interferon-alpha (2) and IFN-alpha (8) to their cell surface
 receptors and neutralizes the antiviral and antiproliferative actions
 of all the type I interferons tested, including IFN-beta ,
 IFN-omega, and human leukocyte IFN, a mixture of different interferon-
 alpha isotypes. Antibody 34F10 recognizes the type I interferon
 receptor with an affinity similar to that of the MAb 64G12 but does
 not inhibit either the binding or the biologic activity of any of the
 type I interferons tested. Both antibodies recognize a protein of
 105 +/- 5 kD from either Daudi or Ly28 cells. Immunoprecipitation
 following surface iodination demonstrated that the neutralizing MAb
 recognizes a protein of 105 kD and the nonneutralizing MAb a protein of
 110 kD in extracts of Daudi cells. A second less intense band was also
 detected by both antibodies. Cross-linking of IFN -alpha (2) to its
 receptor before immunoprecipitation prevented the neutralizing
 antibody from immunoprecipitating the receptor protein, but the
 nonneutralizing MAB was still able to recognize a 140 kD protein
 corresponding to the cross-linked interferon -receptor protein
 complex . Thus, an interferon binding domain appears to be localized
 in a region between amino acids 23 and 229 of the extracellular domain
 of a transmembrane protein that forms part of the type I
 interferon receptor complex containing the epitopes recognized by
 each antibody.

12/3,AB/34 (Item 34 from file: 34)
 DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01957355 Genuine Article#: JP583 (NO REFS KEYED)
 Title: SERUM INTERLEUKIN-2 RECEPTOR AND INTERFERON- ALPHA LEVELS IN A
 PATIENT WITH ALLERGIC GRANULOMATOUS-ANGITIS (CHURG-STRAUSS)
 Author(s): HAYASAKA T; SASAKI H; SUGAWARA T; YASUURA S; KAWAMURA T
 Corporate Source: HAKODATE CHUO HOSP,DEPT INTERNAL MED,33-2 HONCHO/HAKODATE
 040//JAPAN/
 Journal: INTERNAL MEDICINE, 1992, V31, N7 (JUL), P955-959
 ISSN: 0021-5120
 Language: ENGLISH Document Type: ARTICLE
 Abstract: A patient with allergic granulomatous angitis accompanied by
 increases in serum interleukin-2 receptor (IL-2R) and interferon -
 alpha (IFN-alpha) levels is reported. Laboratory findings revealed
 leukocytosis with eosinophilia and increased serum IgE and IgG. The
 serum IL-2R and IFN-alpha were increased. The serum immune complex ,
 interferon -beta , -gamma and complements remained at normal levels.
 The serum IgE, IgG, IL-2R and IFN-alpha correlated with disease
 activity. Immunofluorescent studies using frozen sections obtained from
 the dermal lesion showed no immunoglobulin or complement deposits on
 vascular walls. Measurements of serum IL-2R and IFN-alpha might be
 considered reliable serologic indicators of disease activity.

12/3,AB/89 (Item 3 from file: 349)
 DIALOG(R)File 349:PCT FULLTEXT
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00649150
 IFNAR2/ IFN COMPLEX
 COMPLEXE IFNAR2/IFN
 Patent Applicant/Assignee:
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 MCKENNA Sean; Address - MCKENNA, Sean , 679 Lincoln Street, Ducksberry,
 MA 02332 , US
 Patent and Priority Information (Country, Number, Date):
 Patent: WO 9932141 A1 19990701
 Application: WO 98US26926 19981218 (PCT/WO US9826926)
 Priority Application: US 9768295 19971219
 Designated States: AL; AM; AT; AU; AZ; BA; BG; BR; BY; CA; CH; CN; CU;
 CZ; DE; DK; EE; ES; FI; GB; GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP;
 KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX;
 NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TT; UA; UG;
 UZ; VN; YU; ZW; GM; KE; LS; MW; SD; SZ; UG; ZW; AM; AZ; BY; KG; KZ;
 MD; RU; TJ; TM; AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU;
 MC; NL; PT; SE; BF; BU; CF; CG; CI; CM; GN; GW; ML; MR; NE; SN; TD;
 TG
 Publication Language: English
 Filing Language: English
 Fulltext Word Count: 16598

English Abstract
 The < i> in vivo < /i> effect of Type I interferon (IFN) can be
 prolonged by administering the interferon in the form of a complex with
 an IFN binding chain of the human interferon α ; β ;
 receptor (IFNAR) . Such a complex also improves the stability of the
 IFN and enhances the potency of the IFN . The complex may be a
 non-covalent complex or one in which the IFN and the IFNAR are bound
 by a covalent bond or a peptide. When bound by a peptide bond in the form
 of a fusion protein, the IFN may be separated from the IFNAR by
 means of a peptide linker. Such a fusion protein may be produced by
 recombinant DNA technology. Storing IFN in the form of such a complex
 improves the storage life of the IFN and permits storage under milder
 conditions than would otherwise be possible.

French Abstract
 L'invention concerne la prolongation de l'effet < i> in vivo < /i> de
 l'interferon de type I (IFN) par administration de l'interferon sous
 forme de complexe avec une chaine de liaison d'IFN du recepteur de
 l'interferon humain α ; β ; (IFNAR) . Ce complexe permet
 egalement d'ameliorer la stabilite de l'IFN et augmente la puissance de
 l'IFN. Le complexe peut etre un complexe non covalent ou un complexe dans
 lequel l'IFN et l'IFNAR sont lies par une liaison covalente ou un
 peptide. Lorsqu'ils sont lies par une liaison peptidique sous la forme
 d'une proteine de fusion , l'IFN peut etre separe de l'IFNAR par un
 lien peptidique. On peut produire cette proteine de fusion au moyen
 d'une technique de recombinaison de l'ADN. La conservation de l'IFN sous
 la forme d'un tel complexe permet d'augmenter la duree de conservation de
 l'IFN et de le conserver dans de meilleures conditions qu'il n'aurait etc
 possible autrement.
 ?t 12/ul/92,118,128,129; show files; ds; log hold
 12/3,AB/92 (Item 6 from file: 349)
 DIALOG(R)File 349:PCT FULLTEXT
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00619521
 CHIMERIC INTERLEUKIN-6 SOLUBLE RECEPTOR/LIGAND PROTEIN, ANALOGS THEREOF AND

7/3, AB/4

DIALOG(R)File 154:MEDLINE(R)

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10231462 99421331

Characterization of a soluble ternary complex formed between human interferon- β -la and its receptor chains.

Arduini RM; Strauch KL; Runkel LA; Carlson MM; Hronowski X; Foley SF; Young CN; Cheng W; Hochman PS; Baker DP

Biogen Inc., Cambridge, Massachusetts 02142, USA.

Protein Sci (UNITED STATES) Sep 1999, 8 (9) p1867-77, ISSN 0961-8368

Journal Code: BNV

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The extracellular portions of the chains that comprise the human type I interferon receptor, IFNAR1 and IFNAR2, have been expressed and purified as recombinant soluble His-tagged proteins, and their interactions with each other and with human interferon- β -la (IFN- β -la) were studied by gel filtration and by cross-linking. By gel filtration, no stable binary complexes between IFN- β -la and IFNAR1, or between IFNAR1 and IFNAR2 were detected. However, a stable binary complex formed between IFN- β -la and IFNAR2. Analysis of binary complex formation using various molar excesses of IFN- β -la and IFNAR2 indicated that the complex had a 1:1 stoichiometry, and reducing SDS-PAGE of the binary complex treated with the cross-linking reagent disuccinimidyl glutarate (DSG) indicated that the major cross-linked species had an apparent Mr consistent with the sum of its two individual components. Gel filtration of a mixture of IFNAR1 and the IFN- β -la-IFNAR2 complex indicated that the three proteins formed a stable ternary complex. Analysis of ternary complex formation using various molar excesses of IFNAR1 and the IFN- β -la-IFNAR2 complex indicated that the ternary complex had a 1:1:1 stoichiometry, and reducing SDS-PAGE of the ternary complex treated with DSG indicated that the major cross-linked species had an apparent Mr consistent with the sum of its three individual components. We conclude that the ternary complex forms by the sequential association of IFN- β -la with IFNAR2, followed by the association of IFNAR1 with the preformed binary complex. The ability to produce the IFN- β -la/IFNAR2 and IFN- β -la/IFNAR1/IFNAR2 complexes make them attractive candidates for X-ray crystallography studies aimed at determining the molecular interactions between IFN- β -la and its receptor.

7/3, AB/8

DIALOG(R)File 154:MEDLINE(R)

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09864288 99160899

Formation of a uniquely stable type I interferon receptor complex by interferon β is dependent upon particular interactions between interferon β and its receptor and independent of tyrosine phosphorylation.

K.-Selli-Harde D; Wagner TC; Perez HD; Croze E

Department of Protein Biochemistry, Department of Immunology, Berlex Biosciences, Richmond, California 94804, USA.

Biochem Biophys Res Commun (UNITED STATES) Feb 16 1999, 255 (2)

p539-44, ISSN 0006-291X Journal Code: 9Y8

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Human type I interferons (IFN) require two receptor chains, IFNAR1 and IFNAR2c for high affinity (pM) binding and biological activity. Our previous studies have shown that the ligand dependent assembly of the type I IFN receptor chains is not identical for all type I IFNs. IFN β appears unique in its ability to assemble a stable complex of receptor chains, as demonstrated by the observation that IFNAR2c co-immunoprecipitates with IFNAR1 when cells are stimulated with IFN β but not with IFN α . The characteristics of such a receptor complex are not well defined nor is it understood if differential signaling events can be mediated by variations in receptor assembly. To further characterize the factors required for formation of such a stable receptor complex we demonstrate using IFN stimulated Daudi cells that (1) IFNAR2c co-immunoprecipitates with IFNAR1 even when tyrosine phosphorylation of receptor chains is blocked with staurosporine, and (2)

IFN β but not IFN α 2, is present in the immunoprecipitated receptor complex. These results demonstrate that the unique IFN β induced assembly of type I IFN receptor chains is independent of receptor tyrosine phosphorylation and the recruitment of additional proteins to the receptor by such events. Furthermore, the presence of IFN β in the immunoprecipitated IFN receptor complex suggests that IFN β interacts and binds differently to the receptor than IFN α 2. These results suggest that the specific assembly of type I IFN receptor chains is ligand dependent and may represent an early event which leads to the differential biological responses observed among type I IFNs.

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7/3, AB/42

DIALOG(R)File 154:MEDLINE(R)

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08456288 96075707

Characterization of a domain of a human type I interferon receptor protein involved in ligand binding.

Eid P; Tovey MG

Laboratory of Viral Oncology, CNRS, Villejuif, France.

J Interferon Cytokine Res (UNITED STATES) Mar 1995, 15 (3) p205-11,

ISSN 1079-9907 Journal Code: CD4

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Two monoclonal antibodies that recognize different epitopes of the extracellular domain of one of the proteins that constitute the type I interferon receptor were used to delineate the interferon binding site. Antibody 64G12 both inhibits the binding of radiolabeled interferon- α 2 and IFN- α 8 to their cell surface receptors and neutralizes the antiviral and antiproliferative actions of all the type I interferons tested, including IFN- β , IFN- ω , and human leukocyte IFN, a mixture of different interferon- α isotopes. Antibody 34F10 recognizes the type I interferon receptor with an affinity similar to that of the MAb 64G12 but does not inhibit either the binding or the biologic activity of any of the type I interferons tested. Both antibodies recognize a protein of 105 +/- 5 kD from either Daudi or Ly28 cells. Immunoprecipitation following surface iodination demonstrated that the neutralizing MAB recognizes a protein of 105 kD and the nonneutralizing MAB a protein of 110 kD in extracts of Daudi cells. A second less intense band was also detected by both antibodies. Cross-linking of IFN- α 2 to its receptor before immunoprecipitation prevented the neutralizing antibody from immunoprecipitating the receptor protein, but the nonneutralizing MAB was still able to recognize a 140 kD protein corresponding to the cross-linked interferon-receptor protein complex. Thus, an interferon binding domain appears to be localized in a region between amino acids 23 and 229 of the extracellular domain of a transmembrane protein that forms part of the type I interferon receptor complex containing the epitopes recognized by each antibody.